ECRONICON OPEN ACCESS

EC PAEDIATRICS
Case Report

Osteogenesis Imperfecta Treated with Zoledronic Acid: A Case Report

Ho Chu Mang, Lai Man Hou and Jorge Sales Marques*

Pediatric Department, Cento Hospitalar Conde S. Januário, Macau, China

***Corresponding Author:** Jorge Sales Marques, Pediatric Department, Cento Hospitalar Conde S. Januário, Macau, China.

Received: December 19, 2017; **Published:** January 24, 2018

Abstract

Osteogenesis imperfecta (OI) is a group of inherited connective tissue disorders causing bone fragility and extra-skeletal features. Most OI has mutations in either COL1A1 or COL1A2 which encode for α1 and α2 chains of type I collagen. However, the diagnosis is based on the clinical features. The goals of treatment are reduced fracture rates, improve mobility and life quality. Bisphosphonates are mainstay of pharmacological therapy. We report a case of 33 months old boy diagnosis of OI type IV due to presents of recurrent fractures, blue sclera and hearing impairment. The x-rays showed thin cortex and deformity. No significant finding in the laboratory test. In order to increase the bone mineral density (BMD) and decrease the fracture rate, we prescribe zoledronic acid, which has highly potent efficacy of inhibit bone resorption. BMD control by DEXA, demonstrate significant increase in the lumbar spine and slightly increased in the right hip. Further treatment and follow up are necessary.

Keywords: *Osteogenesis Imperfecta; Zoledronic Acid; DEXA; BMD*

Introduction

Osteogenesis imperfecta (OI), also known as brittle bone disease, is a phenotypically and molecularly heterogeneous group of inherited connective tissue disorders that mainly affect skeletal abnormal causing bone fragility and deformity. Additional extra-skeletal features manifest to a variable degree, including blue sclera, dentinogenesis imperfecta, and hearing loss [1].

Most patients with OI have mutations in either COL1A1 or COL1A2, which encode for α1 and α2 chains of type I collagen, respectively. More recently, mutations in genes involved in post-translational modification of type I collagen, chaperone proteins, signaling molecules, and others undetermined role have been discovered to cause OI [2].

At present, a total of 17 genetic causes of OI have been described with COL1A1 or COL1A2 mutations accounting for a large amount of OI which occurs in 1:15 - 20,000 newborns, more prevalent in populations of European and US [3,4].

The manifestations in OI varies ranges from those with mild disease and few fractures to severe forms with intrauterine fractures and perinatal mortality [5].

There is no available laboratory test for OI. The clinical diagnosis is based on the signs and symptoms; however, skin biopsy and research laboratory have made advances in molecular genetic testing that will be more accessible [6-8].

The goals of treatment are reduced fracture rates, improve mobility and life quality. Bisphosphonates are mainstay of pharmacological therapy for most form of OI. Zoledronic acid is a bisphosphonate that inhibits the bone resorption and bone turnover.

The prognosis depends upon the type of OI. In type IV, fractures are common and will cause deformity and short stature. If we start the treatment as soon as possible, the prognosis will be better with fewer sequels [9].

Case Report

A 33 months old boy presented with recurrent fracture (six times) after birth. The first time was found clavicle fracture when spontaneous delivery, others were found long bone fractures due to fell down from 11 to 30 months old. His prenatal and perinatal history are unremarkable. No family history of hereditary bone, endocrine and developmental diseases. Physical examination found the progressive short stature in growth chart, blue sclera, left femoral deformity and bilateral calcaneal valgus. The laboratory tests of biochemistry, liver, renal, thyroid and parathyroid functions were normal. Urine analysis of biochemistry showed calcium 1.4 mmol/L (N 2.5 - 7.5 mmol/L) and phosphorus 6.61 mmol/L (N 13 - 44 mmol/L). The fractures were on left clavicle fracture (at birth), right ulnar fracture (23 months), left tibia fracture (25 months) and right femoral fracture (30 months) (Figure 1). We don't know the information about the second and third fractures because he was treated in another hospital. The automated auditory brainstem response (AABR) test revealed 20dB (N < 20 dB), mild deafness.

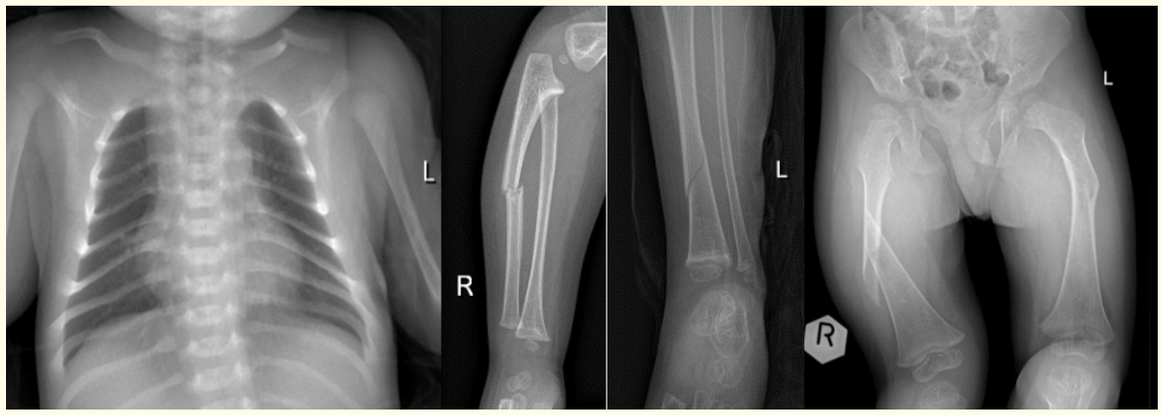

Figure 1: *Fracture sites in the patient.*

The 1st dual-energy x-ray absorptiometry (DEXA) scan was done at 25 months of age. He started treatment then treated with zoledronic acid 0.025 mg/kg at 29 months. We repeated DEXA 3 months later. The result demonstrated increase of 21.5% bone mineral density (BMD) in lumbar spine (L1-L4), increase of 5.9% in right hip, but decrease of 2.9% in left hip, compared to the first DEXA (Figure 2).

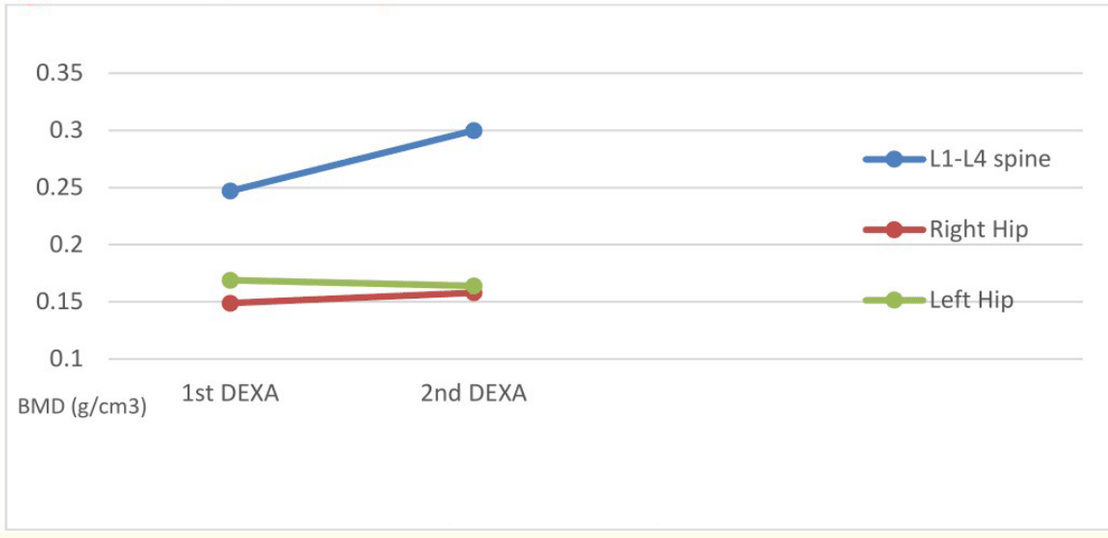

Figure 2: *Comparison of BMD before /after use of zoledronic acid.*

According to guidelines, he was treated with zoledronic acid every 6 months, and follow up in multidisciplinary departments.

Discussion

This is a typical case of OI, type IV. The presents of recurrent fractures after minor injuries, progressive short stature and deformity, extra-skeletal signs of blue sclera and hearing function impairment, no significant finding in the laboratory tests, thin cortisol bone in the radiography, are compatible with this diagnosis.

The consequence of recurrent fractures will result in deformity, short stature, chronic pain and affect the life quality in the future. In order to prevent fracture and decrease the morbidity, multidisciplinary management (e.g. pediatrics, orthopedics, rehabilitation team, stomatologist and otolaryngologist) are necessary for those patients. We decide to treat with bisphosphonates, and control the BMD by DEXA to access the medical efficiency. Children with OI are often treated with intravenous bisphosphonates, which are analogues of pyrophosphate bind to the crystals of hydroxyapatite and inactivate osteoclast cells, therefore preventing bone resorption, and result to less fracture. The form of bisphosphonates includes oral and intravenous, some triad showed both are potent increase the bone mineral density and decrease the risk of fracture incidence in osteogenesis imperfect, furthermore there is no difference between in oral and intravenous administration [10].

The mostly used form with remarkable positive outcomes of intravenous bisphosphonates in osteogenesis imperfecta is pamidronate, but zoledronic acid has recently indicated for the treatment of those patients. Zoledronic acid is a third-generation bisphosphonate, the major advantages of zoledronic acid are its superior antiresorptive potency compared with other bisphosphonates and the treatment interval is every 6 months. In a triad compared the safety and efficacy of zoledronic acid to pamidronate in children with osteogenesis imperfecta, revealed no significant difference in decreased the fracture rate and side effect, but zoledronic acid has more efficacy in BMD [11].

We should familiar with the side effects of zoledronic acid, that includes gastrointestinal symptoms, flu-like symptoms, musculoskeletal pains, hypocalcaemia and hypophosphataemia. Hypotension, liver or renal impairment are very rare.

In this case, we treated with zoledronic acid because of the potent efficacy and longer therapeutic interval. We found significant increased the BMD in L1-L4 spine, slightly increased in right hip and slightly decreased in the left hip after 3 months after treatment. Further studies and follow up are needed, to establish the therapeutic medication and duration.

Conclusion

If we find the patients with recurrent fractures caused by minor trauma, we should suspect of OI. Recurrent fractures can cause deformity, chronic pain and others morbidity. Zoledronic acid could be a choice of treatment.

Bibliography

1. Forlino A., *et al*. "Osteogenesis imperfecta". *Lancet* 387.10028 (2016): 1657-1671.

2. Van Dijk FS., *et al*. "Osteogenesis imperfecta: clinical diagnosis, nomenclature and severity assessment". *American Journal of Medical Genetics Part A* 164A.6 (2014): 1470-1481.

3. Van Dijk FS., *et al*. "EMQN best practice guidelines for the laboratory diagnosis of osteogenesis imperfecta". *European Journal of Human Genetics* 20.1 (2012): 11-19.

4. Ronak M Patel. "A Cross-sectional Multicenter Study of Osteogenesis Imperfecta in North America - Results from the Linked Clinical Research Centers". *Clinical Genetics* 87.2 (2015): 133-140.

5. Marini JC. "Osteogenesis imperfecta". Philadelphia: Saunders (2004).

6. Rauch F and Glorieux FH. "Osteogenesis imperfecta". *Lancet* 363.9418 (2004): 1377-1385.

7. Wenstrup RJ., *et al*. "Distinct biochemical phenotypes predict clinical severity in nonlethal variants of osteogenesis imperfecta". *American Journal of Human Genetics* 46.5 (1990): 975-982.

8. Körkkö J., *et al*. "Analysis of the COL1A1 and COL1A2 genes by PCR amplification and scanning by conformation-sensitive gel electrophoresis identifies only COL1A1 mutations in 15 patients with osteogenesis imperfecta type I: identification of common sequences of null-allele mutations". *American Journal of Human Genetics* 62.1 (1998): 98-110.

9. Singer RB., *et al*. "Mortality in various types of osteogenesis imperfecta". *Journal of Insurance Medicine* 33.3 (2001): 216-220.

10. DiMeglio LA. "Two-year clinical trial of oral alendronate versus intravenous pamidronate in children with osteogenesis imperfecta". *Journal of Bone and Mineral Research* 21.1 (2006): 132-140.

11. Barros ER. "Safety and efficacy of a 1-year treatment with zoledronic acid compared with pamidronate in children with osteogenesis imperfecta". *Journal of Pediatric Endocrinology and Metabolism* 25.5-6 (2012): 485-491.

Volume 7 Issue 2 February 2018